**Supplementary Methods**

*Study population and data sources*

People over the age of 18 years old on kidney replacement therapy (KRT) in Australia and New Zealand between 1965 and 2017 were included in this population-based cohort study. Data regarding demographics, comorbidities, cause of kidney failure [categorised as Fabry disease (FD) versus (vs) non-FD], KRT treatment modality, death, cause of death, graft failure and cause of graft failure were received from Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) in de-identified format. Ethics approvals were obtained from ANZDATA executive (Request ID: 41472) and Royal Brisbane and Women's Hospital Human Research Ethics Committee (LNR/2018/QRBW/46885). Written consent was not obtained as all data received from ANZDATA were fully anonymised prior to analysis. The study was reported in accordance with Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (Table S7)[S6].

People with FD were identified by treating clinicians on ANZDATA data entry based on kidney biopsy results, genetic testing and/or clinical features. The dialysis cohort included all adults who received dialysis either as sole KRT, prior to kidney transplant or after a failed kidney transplant (Figure S1). The transplant cohort included all adults who received a kidney transplant (Figure S1).

*Covariates*

People were classified as pre-enzyme replacement therapy (ERT) era (1 January, 1965 to 31 December, 2000) or post-ERT era (1 January, 2001 to 31 December, 2017) based on the date of commencement of KRT. Age and comorbidities were recorded at the time of dialysis commencement for the dialysis cohort or at the time of kidney transplant in the transplant

cohort. Age was categorised as less than 20 years old, 20-39 years old, 40-59 years old, 60-79 years old, or greater than 80 years old. Comorbidities included diabetes, chronic lung disease, coronary artery disease, peripheral vascular disease and cerebrovascular disease. Ethnicity was categorised as white, Aboriginal and Torres Strait Islander (ATSI), Māori, Asian, or other in the descriptive analyses (Tables S1 and S3) per patient's self-identification and/or clinician identification. Due to a modest number of people in the FD group, ethnicity was categorised as white or other for the Cox regression and competing risk analysis. Dialysis modality was defined as haemodialysis or peritoneal dialysis. Dialysis vintage and transplant era were categorised as shown in Tables S1 and S3.

*Statistical analysis*

Baseline characteristics and medical conditions were summarised using counts and percentages and assessed by $\chi^2$ tests of independence (Table S1). Univariable and multivariable Cox-proportional hazards models were used to evaluate the association between a range of clinical and demographic characteristic and mortality. These analyses were restricted to a contemporary cohort (1 January, 1991 to 31 December, 2017) to minimise the effect of time-related patient and treatment factors. As the focus of this study was on the FD effect, we generated a propensity score based on ethnicity, gender and age to statistically balance the confounding effect of the covariates across the FD classes. For those on dialysis, FD status, age at KRT initiation, gender, smoking status, body mass index (BMI), ethnicity, diabetes status, dialysis modality, dialysis commencement date relative to ERT availability and dialysis vintage were included as covariates. For people who received kidney transplants, FD status, age, gender, smoking status, BMI, ethnicity, diabetes, first KRT modality, KRT commencement date relative to ERT availability, donor source and transplant

era were included as covariates. hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated for each characteristic.

In the transplant cohort, where mortality and graft failure could be considered competing risks, adjusted sub-distribution HRs (ASHRs) were generated using Fine and Gray's proportional hazards model for competing risks [S7]. Any cases with missing observations were excluded from the analyses.

To account for potential confounding effects between the Fabry's groups, we used propensity score regression adjustment. The reason we used the regression adjustment approach as opposed to the more commonly employed propensity score matching or inverse weighting approaches was to retain as much of the sample size as possible (after 4:1 matching there was no gain in retaining additional controls and this would have left us with less than 5% of the original sample). Also, to the best of our knowledge, more advanced propensity score methods have not been developed or implemented for competing risk analysis models. Our propensity score model incorporated patient age, gender and ethnicity effects. Finally, we conducted a sensitivity analysis by stratifying the multivariable Cox-regression analyses by time period to check for potential time bias (particularly with regard to missing variables. All analyses were conducted in R [S8] and the cmprsk R library [S9] was used to perform competing risk analysis.

**Figure S1:** Flow chart demonstrating stratification of patient cohorts. ANZDATA = Australia and New Zealand Dialysis and Transplant registry, FD = Fabry disease, KRT = kidney replacement therapy.

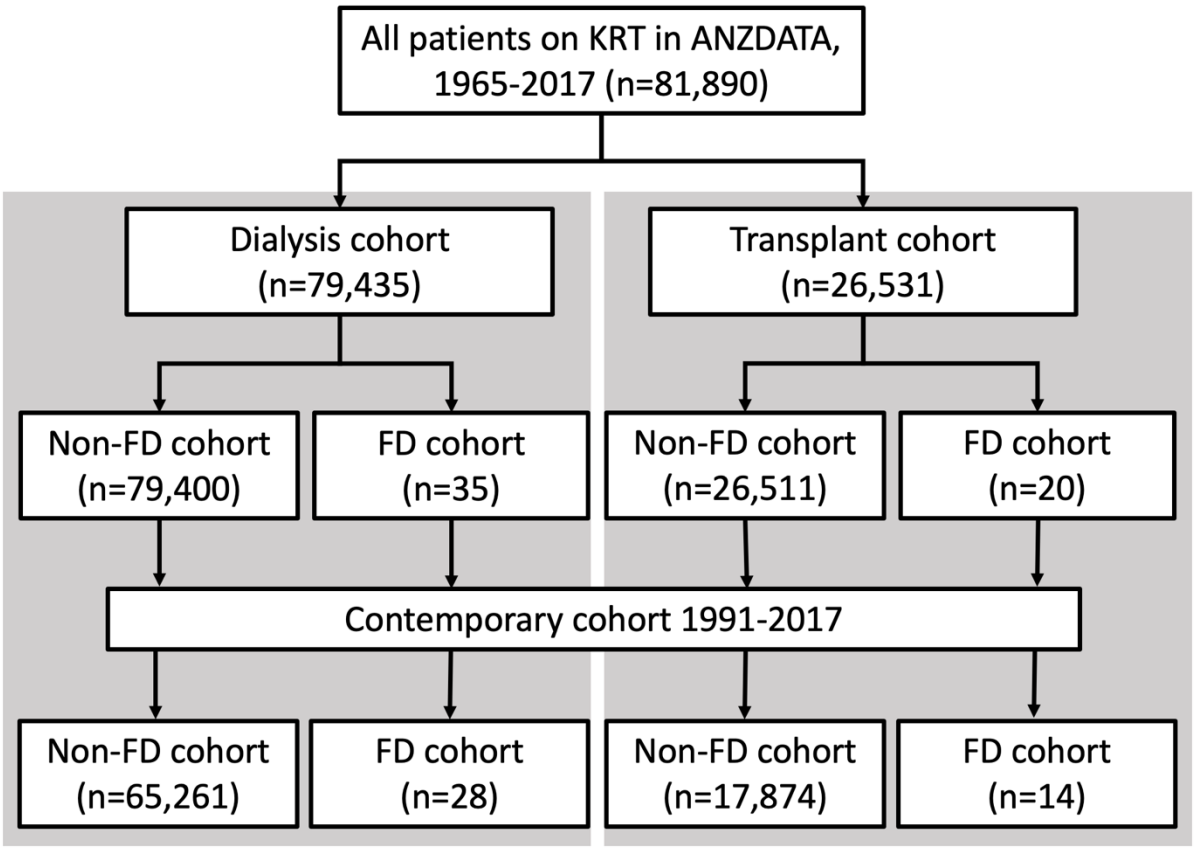

**Table S1:** Socio-demographic characteristics and medical conditions of the Dialysis cohort.

| **Characteristics** | **Non-Fabry disease N=79,400 (%)** | **Fabry disease N=35 (%)** | **P-value** |
|---|---|---|---|
| **Age (years)** | | | 0.002** |
| <20 | 2,361 (3) | 0 | |
| 20-39 | 11,325 (14) | 10 (29) | |
| 40-59 | 28,283 (36) | 19 (54) | |
| 60-79 | 33,325 (42) | 6 (17) | |
| 80+ | 4,106 (5) | 0 | |
| **Gender** | | | 0.003** |
| Female | 32,367 (41) | 5 (14) | |
| Male | 47,033 (59) | 30 (86) | |
| **Smoking status** | | | 0.025** |
| Never | 31,836 (47) | 22 (76) | |
| Former | 26,382 (39) | 5 (17) | |
| Current | 8,930 (13) | 2 (7) | |
| Missing | 12,252 (15) | 6 (17) | |
| **BMI** ($kg/m^2$) | | | 0.008** |
| <18.5 | 3,076 (5) | 2 (7) | |
| 18.5-24.9 | 23,309 (36) | 19 (68) | |
| 25-29.9 | 20,190 (31) | 4 (14) | |
| >30 | 18,832 (29) | 3 (10) | |
| Missing | 13,993 (18) | 7 (20) | |
| **Ethnicity** | | | 0.155 |
| White | 58,189 (73) | 32 (91) | |
| ATSI | 5,549 (7) | 0 (0) | |
| Maori | 7,900 (10) | 0 (0) | |
| Asian | 5,722 (7) | 2 (6) | |
| Other | 1,504 (2) | 1 (3) | |
| Missing | 536 (1) | 0 (0) | |
| **Diabetes** | | | <0.001*** |
| No | 41,548 (52) | 30 (86) | |
| Yes | 29,194 (41) | 1 (3) | |
| Missing | 8,658 (11) | 4 (11) | |
| **Chronic Lung Disease** | | | 0.690 |
| No | 58,622 (74) | 27 (77) | |
| Yes | 10,692 (15) | 3 (10) | |
| Missing | 10,086 (13) | 5 (14) | |
| Coronary Artery Disease | | | 0.249 |
| No | 43,839 (55) | 15 (43) | |
| Yes | 25,604 (37) | 13 (46) | |
| Missing | 9,957 (13) | 7 (20) | |
| Peripheral Vascular Disease | | | 0.693 |
| No | 53,104 (67) | 23 (66) | |
| Yes | 16,208 (23) | 6 (20) | |
| Missing | 10,088 (13) | 6 (17) | |
| Cerebrovascular Disease | | | 0.562 |
| No | 59,986 (76) | 24 (69) | |
| Yes | 9,350 (14) | 6 (20) | |

| | | | |
|---|---|---|---|
| Missing | 10,064 (13) | 5 (14) | |
| **Dialysis modality** | | | 0.960 |
| Haemodialysis | 55,269 (70) | 25 (71) | |
| Peritoneal dialysis | 24,131 (30) | 10 (29) | |
| **Dialysis commencement date relative to ERT availability (2001)** | | | 0.089 |
| Pre ERT | 30,846 (39) | 19 (54) | |
| Post ERT | 48,554 (61) | 16 (46) | |
| **Dialysis vintage** | | | 0.502 |
| 1965-75 | 2,779 (4) | 1 (3) | |
| 1976-85 | 6,478 (8) | 3 (9) | |
| 1986-95 | 11,963 (15) | 7 (20) | |
| 1996-2000 | 9,626 (12) | 8 (23) | |
| 2001-05 | 12,021 (15) | 4 (11) | |
| 2006-10 | 14,228 (18) | 5 (14) | |
| 2011-17 | 22,305 (28) | 7 (20) | |
| **Mortality rate** | | | |
| 1 year mortality | 8,749 (11) | 3 (9) | 0.847 |
| 3 year mortality | 22,556 (28) | 9 (26) | 0.868 |
| 5 year mortality | 32,045 (40) | 15 (43) | 0.897 |
| **Cause of mortality** | | | 0.290 |
| Cardiovascular | 17,715 (22) | 12 (34) | |
| Infection | 6,770 (9) | 2 (6) | |
| Withdrawal | 11,909 (15) | 2 (6) | |
| Cancer | 3,841 (5) | 1 (3) | |
| Other | 10,693 (14) | 7 (20) | |
| Not applicable (did not die) | 28,472 (36) | 11 (31) | |

**Abbreviations**: ATSI = Aboriginal and Torres Strait Islander, BMI = body mass index, ERT = enzyme replacement therapy; Significance level: *<0.05, **<0.01, ***<0.001

**Table S2:** Time stratified analyses for Hazard Ratios and 95% confidence intervals or the association between Fabry disease and mortality for the Dialysis cohort.

| Effect | 1991-95 | | 1996-2000 | | 2001-05 | | 2006-10 | | 2011-17 | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **HR** | **95% CI** | **HR** | **95% CI** | **HR** | **95% CI** | **HR** | **95% CI** | **HR** | **95% CI** |
| **Disease status** | $\chi^2_{(LRT)}$=1.29,df=1,p=0.26 | | $\chi^2_{(LRT)}$=2.37,df=1,p=0.12 | | $\chi^2_{(LRT)}$=0.95,df=1,p=0.33 | | $\chi^2_{(LRT)}$=0.31,df=1,p=0.58 | | $\chi^2_{(LRT)}$=0.63,df=1,p=0.43 | |
| FD | 4.06** | 1.52-10.83 | 1.64 | 0.68-3.95 | 1.32 | 0.33-5.27 | 2.93 | 0.95-9.10 | 2.37 | 0.76-7.35 |
| Non-FD | Reference | - | Reference | - | Reference | - | Reference | - | Reference | - |
| **Smoking status** | $\chi^2_{(LRT)}$=213.06,df=2,p<0.001 | | $\chi^2_{(LRT)}$=255.06,df=2,p<0.001 | | $\chi^2_{(LRT)}$=246.41,df=2,p<0.001 | | $\chi^2_{(LRT)}$=172.24,df=2,p<0.001 | | $\chi^2_{(LRT)}$=116.69,df=2,p<0.001 | |
| Never | Reference | - | Reference | - | Reference | - | Reference | - | Reference | - |
| Former | 1.47*** | 1.38-1.56 | 1.43*** | 1.36-1.50 | 1.37*** | 1.31-1.43 | 1.31*** | 1.26-1.37 | 1.30*** | 1.23-1.38 |
| Current | 1.32*** | 1.22-1.44 | 1.21*** | 1.13-1.29 | 1.18*** | 1.05-1.25 | 1.16*** | 1.09-1.24 | 1.32*** | 1.22-1.42 |
| **BMI** | $\chi^2_{(LRT)}$=71.95,df=3,p<0.001 | | $\chi^2_{(LRT)}$=63.13,df=3,p<0.001 | | $\chi^2_{(LRT)}$=8.56,df=3,p=0.04 | | $\chi^2_{(LRT)}$=4.48,df=3,p=0.21 | | $\chi^2_{(LRT)}$=17.89,df=3,p<0.001 | |
| <18.5 | 0.96 | 0.86-1.08 | 1.04 | 0.94-1.16 | 1.20*** | 1.08-1.34 | 1.13* | 1.00-1.28 | 1.33*** | 1.14-1.54 |
| 18.5-24.9 | Reference | - | Reference | - | Reference | - | Reference | - | Reference | - |
| 25-29.9 | 1.04 | 0.98-1.11 | 0.97 | 0.92-1.02 | 0.93** | 0.88-0.98 | 0.88*** | 0.83-0.93 | 0.88*** | 0.83-0.94 |
| >30 | 1.02 | 0.94-1.11 | 0.95 | 0.89-1.01 | 0.84*** | 0.80-0.89 | 0.74*** | 0.70-0.78 | 0.70*** | 0.66-0.75 |
| **Diabetes** | $\chi^2_{(LRT)}$=506.22,df=1,p<0.001 | | $\chi^2_{(LRT)}$=737.43,df=1,p<0.001 | | $\chi^2_{(LRT)}$=785.31,df=1,p<0.001 | | $\chi^2_{(LRT)}$=808.73,df=1,p<0.001 | | $\chi^2_{(LRT)}$=357.56,df=1,p<0.001 | |
| Yes | 1.72*** | 1.61-1.83 | 1.65*** | 1.57-1.73 | 1.52*** | 1.45-1.59 | 1.59*** | 1.52-1.66 | 1.47*** | 1.39-1.56 |
| No | Reference | - | Reference | - | Reference | - | Reference | - | Reference | - |
| **Dialysis modality** | $\chi^2_{(LRT)}$=26.57,df=1,p<0.001 | | $\chi^2_{(LRT)}$=23.46,df=1,p<0.001 | | $\chi^2_{(LRT)}$=0.03,df=1,p=0.87 | | $\chi^2_{(LRT)}$=21.60,df=1,p<0.001 | | $\chi^2_{(LRT)}$=77.82,df=1,p<0.001 | |
| HD | Reference | - | Reference | - | Reference | - | Reference | - | Reference | - |
| PD | 1.11*** | 1.05-1.17 | 1.08** | 1.03-1.14 | 1.01 | 0.96-1.06 | 0.90*** | 0..86-0.95 | 0.80*** | 0.75-0.84 |
| Transplant | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA |
| **Missing observations** | 620 | | 73 | | 56 | | 93 | | 893 | |

**Abbreviations**: ATSI = Aboriginal and Torres Strait Islander, BMI = body mass index, CI = confidence interval, FD = Fabry disease, HD = haemodialysis, HR = hazard ratio, NA = not applicable, PD = peritoneal dialysis; Significance level: *<0.05, **<0.01, ***<0.001

**Table S3:** Socio-demographic characteristics and medical conditions of the Transplant cohort.

| **Characteristics** | **Non-Fabry disease N=26,511 (%)** | **Fabry disease N=20 (%)** | **P-value** |
|---|---|---|---|
| **Age (years)** | | | 0.571 |
| <20 | 2,381 (9) | 0 (0) | |
| 20-39 | 8,689 (33) | 8 (40) | |
| 40-59 | 12,642 (48) | 11 (55) | |
| 60-79 | 2,798 (11) | 1 (5) | |
| 80+ | 1 (0) | 0 (0) | |
| **Gender** | | | 0.014* |
| Female | 10,426 (39) | 2 (10) | |
| Male | 16,085 (61) | 18 (90) | |
| **Smoking status** | | | 0.744 |
| Never | 11,846 (59) | 11 (73) | |
| Former | 6,006 (30) | 3 (20) | |
| Current | 2,163 (11) | 1 (7) | |
| Missing | 6,496 (25) | 5 (25) | |
| **BMI (**$kg/m^2$) | | | 0.422 |
| <18.5 | 1,530 (8) | 0 (0) | |
| 18.5-24.9 | 8,061 (43) | 9 (64) | |
| 25-29.9 | 5,766 (31) | 2 (14.) | |
| >30 | 3,466 (18) | 3 (21) | |
| Missing | 7,688 (29) | 6 (30) | |
| **Ethnicity** | | | 0.413 |
| White | 21,659 (82) | 19 (95) | |
| ATSI | 700 (2) | 0 (0) | |
| Maori | 1,320 (5) | 0 (0) | |
| Asian | 2,186 (8) | 0 (0) | |
| Other | 452 (2) | 1 (5) | |
| Missing | 194 (0) | 0 (0) | |
| **Diabetes** | | | 0.185 |
| No | 18,714 (71) | 17 (85) | |
| Yes | 3,696 (17) | 0 (0) | |
| Missing | 4,101 (16) | 3 (15) | |
| **Chronic Lung Disease** | | | 0.315 |
| No | 20,822 (78) | 15 (75) | |
| Yes | 970 (5) | 2 (12) | |
| Missing | 4,719 (18) | 3 (15) | |
| **Coronary Artery Disease** | | | 0.008** |
| No | 19,531 (74) | 10 (50) | |
| Yes | 2,044 (10) | 5 (33) | |
| Missing | 4,936 (19) | 5 (25) | |
| **Peripheral Vascular Disease** | | | 0.460 |
| No | 20,535 (78) | 14 (70) | |
| Yes | 1,184 (6) | 2 (13) | |
| Missing | 4,792 (18) | 4 (20) | |
| **Cerebrovascular Disease** | | | <0.001*** |
| No | 21,111 (80) | 12 (60) | |
| Yes | 684 (3) | 5 (29) | |
| Missing | 4,716 (18) | 3 (15) | |

| | | | |
|---|---|---|---|
| **First KRT modality** | | | 0.460 |
| Haemodialysis | 16,322 (62) | 15 (75) | |
| Peritoneal dialysis | 7,746 (29) | 4 (20) | |
| Pre-emptive transplant | 2,443 (9) | 1 (5) | |
| **KRT commencement date relative to ERT availability (2001)** | | | |
| Pre ERT | 14,463 (55) | 14 (70) | 0.245 |
| Post ERT | 12,048 (45) | 6 (30) | |
| **Donor source** | | | 1.000 |
| Deceased | 19,311 (73) | 15 (75) | |
| Live donor | 7,200 (27) | 5 (25) | |
| **Transplant era** | | | 0.534 |
| 1965-75 | 1,931 (3) | 1 (5) | |
| 1976-85 | 3,469 (13) | 2 (10) | |
| 1986-95 | 4,623 (17) | 4 (20) | |
| 1996-2000 | 2,702 (10) | 3 (15) | |
| 2001-05 | 3,189 (12) | 5 (25) | |
| 2006-10 | 3,810 (14) | 1 (5) | |
| 2011-17 | 6,787 (26) | 4 (20) | |
| **Mortality rate** | | | |
| 1 year mortality | 1,564 (6) | 2 (10) | 0.762 |
| 3 year mortality | 2,676 (10) | 3 (15) | 0.721 |
| 5 year mortality | 3,707 (14) | 4 (20) | 0.651 |
| **Cause of mortality** | | | 0.288 |
| Cardiovascular | 3,169 (12) | 5 (25) | |
| Infection | 1,989 (8) | 2 (10) | |
| Withdrawal | 891 (3) | 0 (0) | |
| Cancer | 1,868 (7) | 1 (5) | |
| Other | 3,073 (12) | 4 (20) | |
| Did not die | 15,521 (59) | 8 (40) | |
| **Graft failure rate** | | | |
| 1 year graft failure | 2,829 (11) | 2 (10) | 1.00 |
| 3 year graft failure | 3,735 (14) | 2 (10) | 0.838 |
| 5 year graft failure | 4,496 (17) | 2 (10) | 0.595 |
| **Cause of graft failure** | | | 0.877 |
| Rejection (acute + hyperacute) | 1,721 (7) | 0 (0) | |
| Chronic allograft nephropathy | 4,251 (16) | 2 (10) | |
| Vascular | 598 (2) | 0 (0) | |
| Technical | 226 (1) | 0 (0) | |
| Glomerulonephritis | 444 (2) | 0 (0) | |
| Non-compliance | 232 (1) | 0 (0) | |
| Other | 641 (2) | 1 (5) | |
| No failure | 18,398 (69) | 17 (85) | |
| **Disease in graft kidney** | | | 0.877 |
| BK virus nephropathy | 396 (2) | 20 (100) | |
| De novo glomerulonephritis | 211 (1) | 0 (0) | |
| Glomerulonephritis in graft | 111 (1) | 0 (0) | |
| Disease recurrence | 790 (3) | 0 (0) | |
| **Abbreviations**: ATSI = Aboriginal and Torres Strait Islander, BMI = body mass index, ERT = enzyme replacement therapy; Significance level: *<0.05, **<0.01, ***<0.001 | | | |

**Table S4:** Time stratified analyses for Hazard Ratios and 95% confidence intervals for the association between Fabry disease and mortality for the Transplant cohort.

| Effect | 1991-95 | | 1996-2000 | | 2001-05 | | 2006-10 | | 2011-17 | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **HR** | **95% CI** | **HR** | **95% CI** | **HR** | **95% CI** | **HR** | **95% CI** | **HR** | **95% CI** |
| **Disease status** | $\chi^2_{(LRT)}$=1.93,df=1,p=0.16 | | $\chi^2_{(LRT)}$=4.61,df=1,p=0.03 | | $\chi^2_{(LRT)}$=0.45,df=1,p=0.50 | | $\chi^2_{(LRT)}$=0.54,df=1,p=0.46 | | $\chi^2_{(LRT)}$=2.64,df=1,p=0.10 | |
| FD | 4.63 | 0.64-33.27 | 6.88*** | 2.20-21.52 | 0.78 | 0.11-5.63 | NA | NA | 12.00* | 1.67-86.38 |
| Non-FD | Reference | - | Reference | - | Reference | - | Reference | - | Reference | - |
| **Smoking status** | $\chi^2_{(LRT)}$=36.45,df=2,p<0.001 | | $\chi^2_{(LRT)}$=107.51,df=2,p<0.001 | | $\chi^2_{(LRT)}$=68.60,df=2,p<0.001 | | $\chi^2_{(LRT)}$=57.62,df=2,p<0.001 | | $\chi^2_{(LRT)}$=25.83,df=2,p<0.001 | |
| Never | Reference | - | Reference | - | Reference | - | Reference | - | Reference | - |
| Former | 1.33** | 1.12-1.58 | 1.59*** | 1.40-1.81 | 1.57*** | 1.36-1.81 | 1.45*** | 1.22-1.72 | 1.19 | 0.95-1.49 |
| Current | 1.37** | 1.09-1.72 | 1.74*** | 1.46-2.07 | 1.54*** | 1.27-1.86 | 1.77*** | 1.42-2.21 | 1.90*** | 1.40-2.56 |
| **BMI** | $\chi^2_{(LRT)}$=50.60,df=3,p<0.001 | | $\chi^2_{(LRT)}$=38.99,df=3,p<0.001 | | $\chi^2_{(LRT)}$=38.86,df=3,p<0.001 | | $\chi^2_{(LRT)}$=13.77,df=3,p=0.003 | | $\chi^2_{(LRT)}$=13.49,df=3,p=0.004 | |
| <18.5 | 0.61** | 0.4-0.84 | 0.78 | 0.59-1.02 | 0.73 | 0.53-1.02 | 1.02 | 0.70-1.49 | 0.80 | 0.44-1.46 |
| 18.5-24.9 | Reference | - | Reference | - | Reference | - | Reference | - | Reference | - |
| 25-29.9 | 1.34** | 1.12-1.60 | 1.30*** | 1.12-1.49 | 0.20* | 1.03-1.39 | 1.23* | 1.02-1.48 | 1.02 | 0.79-1.31 |
| >30 | 1.60*** | 1.55-2.04 | 1.29** | 1.08-1.54 | 1.48*** | 1.23-1.77 | 1.30* | 1.06-1.59 | 1.29 | 1.00-1.67 |
| **Diabetes** | $\chi^2_{(LRT)}$=36.75,df=1,p<0.001 | | $\chi^2_{(LRT)}$=117.60,df=1,p<0.001 | | $\chi^2_{(LRT)}$=92.85,df=1,p<0.001 | | $\chi^2_{(LRT)}$=79.95,df=1,p<0.001 | | $\chi^2_{(LRT)}$=30.18,df=1,p<0.001 | |
| Yes | 1.91*** | 1.55-2.37 | 2.17*** | 1.88-2.51 | 2.02*** | 1.73-2.35 | 2.09*** | 1.76-2.48 | 1.75*** | 1.40-2.17 |
| No | Reference | - | Reference | - | Reference | - | Reference | - | Reference | - |
| **Dialysis modality** | $\chi^2_{(LRT)}$=15.16,df=1,p<0.001 | | $\chi^2_{(LRT)}$=53.27,df=2,p<0.001 | | $\chi^2_{(LRT)}$=39.63,df=2,p<0.001 | | $\chi^2_{(LRT)}$=46.45,df=2,p<0.001 | | $\chi^2_{(LRT)}$=8.23,df=2,p=0.02 | |
| HD | Reference | - | Reference | - | Reference | - | Reference | - | Reference | - |
| PD | 1.12 | 0.95-1.33 | 1.02 | 0.90-1.17 | 0.97 | 0.83-1.12 | 0.86 | 0.72-1.03 | 0.98 | 0.78-1.23 |
| Transplant | 0.77 | 0.55-1.09 | 0.49*** | 0.36-0.67 | 0.55*** | 0.41-0.73 | 0.45*** | 0.33-0.63 | 0.86 | 0.54-1.39 |
| **Donor source** | $\chi^2_{(LRT)}$=33.07,df=1,p<0.001 | | $\chi^2_{(LRT)}$=44.04,df=1,p<0.001 | | $\chi^2_{(LRT)}$=20.49,df=1,p<0.001 | | $\chi^2_{(LRT)}$=16.06,df=1,p<0.001 | | $\chi^2_{(LRT)}$=21.54,df=1,p<0.001 | |
| Deceased | Reference | - | Reference | - | Reference | - | Reference | - | Reference | - |
| Live donor | 0.56*** | 0.45-0.69 | 0.62*** | 0.54-0.72 | 0.72*** | 0.63-0.84 | 0.71*** | 0.59-0.84 | 0.51*** | 0.37-0.69 |
| **Missing observations** | 667 | | 1130 | | 942 | | 655 | | 372 | |

**Abbreviations**: ATSI = Aboriginal and Torres Strait Islander, BMI = body mass index, FD = Fabry disease, HD = haemodialysis, HR = hazard ratios, NA = not applicable, PD = peritoneal dialysis; Significance level: *<0.05, **<0.01, ***<0.001

**Table S5:** Competing risk analysis – adjusted Sub-distribution Hazard Ratios and 95% confidence intervals for death-censored graft failure and graft failure-censored mortality risk.

| | Graft failure | | Mortality | |
|---|---|---|---|---|
| **Effect** | **ASHR** | **95% CI** | **ASHR** | **95% CI** |
| **Disease status** | | | | |
| Fabry's disease | 0.92 | 0.13-6.46 | 3.27* | 1.30-8.25 |
| Non-Fabry's disease | Reference | - | Reference | - |
| **Smoking status** | | | | |
| Never | Reference | - | Reference | - |
| Former | 1.35*** | 1.19-1.52 | 1.45*** | 1.32-1.58 |
| Current | 1.77*** | 1.52-2.07 | 1.46*** | 1.29-1.66 |
| **BMI** | | | | |
| <18.5 | 1.02 | 0.81-1.29 | 0.62*** | 0.50-0.77 |
| 18.5-24.9 | Reference | - | Reference | - |
| 25-29.9 | 1.30*** | 1.14-1.47 | 1.18*** | 1.08-1.29 |
| >30 | 1.40*** | 1.20-1.63 | 1.29*** | 1.15-1.44 |
| **Diabetes** | | | | |
| Yes | 1.92*** | 1.69-2.19 | 0.83 | 0.70-0.99 |
| No | Reference | - | Reference | - |
| **First KRT modality** | | | | |
| Haemodialysis | Reference | - | Reference | - |
| Peritoneal dialysis | 1.07 | 0.95-1.21 | 0.95 | 0.87-1.04 |
| Pre-emptive transplant | 0.73** | 0.57-0.92 | 0.54*** | 0.45-0.66 |
| **KRT commencement date relative to ERT availability (2001)** | | | | |
| Pre ERT | 1.61*** | 1.29-2.00 | 1.78 | 1.61-1.96 |
| Post ERT | Reference | - | Reference | - |
| **Donor source** | | | | |
| Deceased | Reference | - | Reference | - |
| Live donor | 0.72*** | 0.63-0.83 | 0.65 | 0.59-0.72 |
| **Transplant era** | | | | |
| 1991-1995 | Reference | - | Reference | - |
| 1996-2000 | 0.77*** | 0.66-0.89 | 1.08 | 0.95-1.23 |
| 2001-05 | 0.59*** | 0.50-0.71 | 1.04 | 0.90-1.19 |
| 2006-10 | 0.31*** | 0.23-0.41 | 0.97 | 0.84-1.12 |
| 2011-17 | 0.15 | 0.11-0.21 | N/A | N/A |

**Abbreviations**: ASHR = adjusted subdistribution hazard ratio, ATSI = Aboriginal and Torres Strait Islander, BMI = body mass index, CI = confidence intervals, ERT = enzyme replacement therapy, KRT = kidney replacement therapy; Significance level: *<0.05, **<0.01, ***<0.001

**Table S6:** Comparison to published clinical outcomes in other registry-based FD populations.

| Population | Years of recruitment | N | Dialysis | Transplant | | Comments |
|---|---|---|---|---|---|---|
| | | | Mortality rate | Mortality rate | Graft failure rate | |
| ANZDATA (this study) | 1965-2017 | 35D<br>20T | 1 year = 9%<br>3 year = 26%<br>5 year = 43% | 1 year = 10%<br>3 year = 15%<br>5 year = 20% | 1 year = 10%<br>3 year = 10%<br>5 year = 10% | Increased mortality risk in D/T populations compared to non-FD counterparts. Similar graft failure rates |
| USRDS [S10] | 1985-1993 | 42D[a]<br>95D[b] | 3 year = 30%[a]<br>3 year = 37%[b] | NR | NR | Trend towards increased mortality in people with FD on dialysis compared to non-diabetic controls |
| USRDS [S11] | 1988-1998 | 93T | NR | 5 year = 17% | 1 year = 9%<br>5 year = 24% | Equivalent 5 year patient and graft survival compared to matched controls |
| OPTN [S12] | 1987-2007 | 197T | NR | 5 year = 19% | 5 year = 26% | FD cohort had inferior 5 year survival on matched cohort analysis. Similar graft survival compared to non-FD cohort |
| ERA-EDTA [S13] | 1985-1993 | 83 D/T<br>33T | 5 year = 59% | NR | 3 year = 33% | Similar post-transplant survival compared to those <55 years old with standard primary renal disease |
| Fabry Registry, Fabry Outcome Survey, RIDT (Italian) [S14] | NR | 17D<br>17T | 6 year = 41% | 6 year = 0% | 6 year = 12% | All patients on ERT |
| Fabry Outcome Survey [S15] | 2001-2006 | 36T | NR | Total = 11% | Total = 8% | Contains people who received and did not receive ERT. Mean follow-up time 7.7 years |
| FD kidney transplant recipients in Zurich, Bern, Lausanne, Switzerland; Berlin, Germany [S1] | 1979-2017 | 17T | NR | 5 year = 0%<br>10 year = 0 %<br>15 year = 33%<br>18 year = 56%<br>20 year = 75% | 5 year = 7%<br>10 year = 8%<br>15 year = 40%<br>18 year = 60%<br>20 year = 78% | Median follow-up time 11.5 years. 14/17 received ERT. Similar graft survival and superior death-censored graft survival compared to matched controls |

**Abbreviations**: ANZDATA = Australia and New Zealand Dialysis and Transplant Registry, D = dialysis, ERA-EDTA = European Renal Association-European Dialysis and Transplant Association, ERT = enzyme replacement therapy, FD = Fabry disease NR = not reported, OPTN = Organ Procurement Transplant Network, RIDT = Registro Italiano Dialisi e Trapianto, T = transplant, USRDS = United States Renal Data System

[a] 1995-1998, [b] 1985-1993

**Table S7:** modified STROBE statement.

| | Item No | Recommendation |
|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract ☒ |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found ☒ |
| **Introduction** | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported ☒ |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses ☒ |
| **Methods** | | |
| Study design | 4 | Present key elements of study design early in the paper ☒ |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection ☒ |
| Participants | 6 | (*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up ☒<br>*Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls<br>*Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable ☒ |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement) ☒ |
| Bias | 9 | Describe any efforts to address potential sources of bias ☒ |
| Study size | 10 | Explain how the study size was arrived at (if applicable) (N/A) |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why ☒ |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding ☒ |
| | | (*b*) Describe any methods used to examine subgroups and interactions ☒ |
| | | (*c*) Explain how missing data were addressed ☒ |
| | | (*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed ☒<br>*Case-control study*—If applicable, explain how matching of cases and controls was addressed<br>*Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy |
| | | (*e*) Describe any sensitivity analyses ☒ |
| **Results** | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed ☒ |
| | | (c) **Use of a flow diagram** |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders ☒ |
| | | (b) Indicate number of participants with missing data for each variable of interest ☒ |

| | | |
|---|---|---|
| | | (c) *Cohort study*—Summarise follow-up time (eg, average and total amount) ☒ |
| Outcome data | 15* | *Cohort study*—Report numbers of outcome events or summary measures over time ☒ |
| | | *Case-control study*—Report numbers in each exposure category, or summary measures of exposure |
| | | *Cross-sectional study*—Report numbers of outcome events or summary measures |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included ☒ |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses ☒ |
| **Discussion** | | |
| Key results | 18 | Summarise key results with reference to study objectives ☒ |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias ☒ |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence ☒ |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results ☒ |

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

**Supplementary References**


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S4. Mignani R, Panichi V, Giudicissi A*, et al.* Enzyme replacement therapy with agalsidase beta in kidney transplant patients with Fabry disease: a pilot study. *Kidney Int* 2004; **65:** 1381-1385.

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S7. Fine JP, Gray RJ. A Proportional Hazards Model for the Subdistribution of a Competing Risk. *J Am Stat Assoc* 1999; **94:** 496-509.

S8. R Core Team: R: A language and environment for statistical computing. In (vol 2020), Vienna, Austria, R Foundation for Statistical Computing, 2020

S9. Gray B: cmprsk: Subdistribution Analysis of Competing Risks. In, R package version 2.2-10 ed, 2020

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S13. Tsakiris D, Simpson HKL, Jones EHP*, et al.* Rare diseases in renal replacement therapy in the ERA-EDTA Registry. *Nephrol Dial Transplant* 1996; **11:** 4-20.

S14. Mignani R, Feriozzi S, Pisani A*, et al.* Agalsidase therapy in patients with Fabry disease on renal replacement therapy: a nationwide study in Italy. *Nephrol Dial Transplant* 2007; **23:** 1628-1635.

S15. Cybulla M, Walter KN, Schwarting A*, et al.* Kidney transplantation in patients with Fabry disease. *Transpl Int* 2009; **22:** 475-481.